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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,716	10/15/2001	Mark I. Greene	UPN0015-103	4425

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Pepper Hamilton LLP
400 Berwyn Park
899 Cassatt Road
Berwyn, PA 19312-1183

EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/977,716	GREENE ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15,16 and 18-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,15,16 and 18-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/02/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/07 has been entered.

2. The response filed 9/10/07 to the Office action has been entered. Claims 1, 15-16 and 18-33 are pending.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1, 15-16, and 18-33 respectively remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 7,045,286, over claims 1-2, 4, and 12-18 of copending Application No. 10/856,057 and over claims 1-4 of copending Application No. 10/333542 as set forth in the office action mailed 9/21/06 because the terminal disclaimer was not filed.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 15-16 and 18-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Since the newly added phrase "unlabeled" to RNA product has no support in the specification, it constitutes a new matter.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 15-16 and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kacian et al. (5,888,729 issued Mar 30, 1999) in view of Eberwine et al. (5,922,553, issued 7/13/1999), Fields et al. (WO 94/26932, issued November 24, 1994) and Waggoner (5,627,027, issued May 6, 1997).

Kacian et al. disclose a method for detect and/or quantitate a specific nucleic acid target sequence in a sample (See column 3, lines 45-49). The method produces a RNA-promoter driven cDNA sequence, which is used to produce RNA copies (See column 4, lines 30-45 and column 9, lines 25-39).

Kacian et al. do not disclose the RNA-promoter driven cDNA, which is coupled, to an antibody for the protein detection or quantification by immuno aRNA.

Eberwine et al. disclose a method, which is for detecting a selected protein by immuno aRNA (See column, 2, lines, 37-50). The presence and quantity of labeled RNA transcript is indicative of the amount of selected protein present (See column 4, lines 33-36 and columns 7-8, claims 1-2). In the method a first antibody targeted to the selected protein is immobilized to a solid support. A RNA-promoter driven cDNA sequence is covalently coupled to a second antibody, which binds the selected protein (See column 2, lines 37-51). The cDNA is double stranded (See column 5, lines 34-35) for use as a template for T7 RNA polymerase (see column 4, lines 41-42). The technique of a RNA synthesis is explicitly disclosed (See column 3, lines 9-24). First strand synthesis proceeds with the addition of AMV-reverse transcriptase (See column 4, lines 50-51). The presence and quantity of labeled RNA transcript is indicative of the amount of selected protein present (See column 4, lines 33-36).

One of ordinary skill in the art would have been motivated to use the RNA-promoter driven cDNA as produced by the method of Kacian et al. to couple to an antibody because Eberwine et al. taught coupling the RNA-promoter driven cDNA to an antibody (See column 5, lines 65-67 and column 6, lines 1-6) used in a method of immuno aRNA (See column 2, lines 44-50) and the RNA-promoter driven cDNA of Kacian et al. produces large number of RNA (See column 4, lines 30-45 and column 9, lines 25-39).

However, by using the method of Kacian et al. to produce RNA, the amplified RNA of Kacian et al. is unlabled and Kacian et al. do not disclose using fluorescent dye to stain the unlabeled amplified RNA and that the fluorescent dye is cyanine dye.

Waggoner discloses that cyanine dye can be used to attach to fragments of DNA or RNA to identify the presence and quantity of specific nucleotide sequence in samples of DNA or RNA (See column 8, lines 51-56).

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply fluorescent dye, cyanine dye to stain the unlabeled amplified RNA of Kacian et al. for detecting and/or quantifying molecules expressing a selected epitope in a sample because as indicated by Waggoner, cyanine dye is highly light absorbing dye molecules to nucleic acid and can be used for detection and quantification in very low amounts (See column 4, lines 35-45) It would have been prima facie obvious to apply cyanine dye for detecting or quantifying molecule expressing a selected epitope in a sample.

Eberwine et al. and Kacian et al. also do not disclose that biotin is located at the 5' terminus of the oligonucleotide and biotin-streptavidin linker is used in attaching between the monoclonal antibody and the oligonucleotide.

Fields et al. disclose nucleic acid tagged immunoassay. The method involves an oligonucleotide linked to a ligand bound to an antigen in a specimen from a subject and detecting the presence of the oligonucleotide indicating the presence of the antigen in the subject (See pg. 2, lines 14-25). Biotin-streptavidin linker is used in linking the oligonucleotide to the ligand (See pg. 5, lines 5-12). The oligonucleotide is amplified by polymerase chain reaction prior to detection (See pg. 5, lines 31-34). The oligonuleotide is biotinylated at 5' terminus (See pg. 15, lines 24-29). Other method of detecting the presence of the oligonucleotide include the detection of RNA transcripts generated from the oligonucleotide using RNA polymerase (See pg. 6, lines 27-29).

One of ordinary skill in the art at the time of the instant invention would have also been motivated to apply the biotin-streptavidin as linker for attaching the oligonucleotide to the monoclonal antibody as taught by Fields et al. because the method of Fields et al. can be used in detecting very small quantities of antigen and antibody (See pg. 7, lines 22-25). It would have been prima facie obvious to apply the linker biotin-streptavidin for attaching the oligonucleotide to the monoclonal antibody for detecting or quantifying molecules expressing a selected epitope in a sample.

The response filed 9/10/07 argues that the combination of references does not produce the claimed invention in that the methods of Kacian et al., Eberwine et al., Waggoner and Fields et al. are described. However, the teachings of Kacian et al. are applied herein because Kacian et al. disclose that a nucleic acid sequence comprising a promoter sequence is used as a template to produce multiple RNA copies by an RNA polymerase (See column 4, Lines 30-54). Eberwine et al. disclose that the presence and quantity of labeled RNA transcript is indicative of the amount of selected protein present (See column 4, lines 33-36 and columns 7-8, claims 1-2) and a RNA-promoter driven cDNA sequence is covalently coupled to a second antibody, which binds the selected protein (See column 2, lines 37-51). Nevertheless, the RNA amplified were not labeled by using the method of Kacian et al. and Kacian et al. do not disclose using fluorescent dye to stain the unlabeled amplified RNA. Waggoner discloses that cyanine dye can be used to attach to fragments of DNA or RNA to identify the presence and quantity of specific nucleotide sequence in samples of DNA or RNA (See column 8, lines 51-56). Field et al. disclose that biotin-streptavidin linker is used in linking the oligonucleotide to the ligand (See pg. 5, lines 5-12).

The response argues that staining RNA and labeling RNA is different. However, the phrase "stain" or "label" is not defined in the specification. The phrase "stain" and "label is interpreted as having the same meaning.

Therefore based upon the analysis above, with the motivation as set forth in the rejection, these references are applied again.

Allowable Subject Matter

9. The following is a statement of reasons for the indication of allowable subject matter:

Concerning claims 23-33, no prior art has been found teaching or suggesting a method for quantifying molecules expressing a selected epitope in a sample comprising a step of measuring a quanta of fluorescence signals emitted from the stained amplified unlabeled RNA product which is directly proportional to epitope detector bound to the surface and molecules expressing the selected epitope in the sample.

There is no motivation to combine the cited references to render the step of measuring a quanta of fluorescence signals emitted from stained unlabeled RNA product which is directly proportional to epitope detector bound to the surface and molecules expressing the selected epitope in the sample as claimed in claim23.

Summary

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Joyce Tung
January 22, 2008

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
1/24/08